Dkt. 43966-CB/JPW/SHS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Graham P. Allaway et al.

Serial No. : Not Yet Known (continuation of U.S. Serial No. 08/973,601, filed March 16, 1998)

Filed : July 12, 2001

For : METHODS FOR USING RESONANCE ENERGY TRANSFER-BASED ASSAY OF HIV-1 ENVELOPE GLYCOPROTEIN-MEDIATED MEMBRANE FUSION, AND KITS FOR PRACTICING SAME

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July 12, 2001

Assistant Commissioner for Patents
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ATTN: Box Patent Applications

SIR:

PRELIMINARY AMENDMENT

Please amend the subject application as follows:

In the specification:

On page 1, lines 6-9, please delete the paragraph beginning "This application is a continuation-in-part" and insert the following paragraph

> --This application is a continuation of U.S. Serial No. 08/973,601, filed March 16, 1998, which is a national stage application filed in 35 U.S.C. §371 of PCT/US96/09894, filed June 7, 1996, which is a continuation-in-part of U.S. Serial No. 08/475,515, filed June 7, 1995, now abandoned.--

In the claims:

Please cancel claims 1-6 without prejudice or disclaimer to applicants right to pursue the subject matter of these claims in

a later-filed application and add new claims 7-12 as follows:

--7. (New) A method of inhibiting fusion of a macrophage-tropic primary isolate of HIV-1 to a $CD4^+$ cell susceptible to infection by a macrophage-tropic primary isolate of HIV-1 which comprises contacting the CD4+ cell with an effective amount of an agent which is (1) capable of inhibiting fusion of a macrophage-tropic primary isolate of HIV-1 to a $CD4^+$ cell susceptible to infection by a macrophage-tropic primary isolate of HIV-1, but (2) not capable of inhibiting fusion of a T cell-tropic isolate of HIV-1 to a $CD4^+$ cell susceptible to infection by a T cell-tropic isolate of HIV-1, thereby inhibiting the fusion of the macrophage-tropic primary isolate of HIV-1 to the $CD4^+$ cell.--

--8. (New) The method of claim 7, wherein the agent is determined to be capable of inhibiting fusion of a macrophage-tropic primary isolate of HIV-1 to a $CD4^+$ cell but not capable of inhibiting fusion of a T cell-tropic isolate of HIV-1 to a CD4+ cell using a method which comprises:

(a) contacting (i) a first appropriate $CD4^+$ cell, which is labeled with a first dye, with (ii) a cell expressing an HIV-1 envelope glycoprotein of the macrophage-tropic primary isolate of HIV-1 on its surface, which is labeled with a second dye, in the presence of an excess of the agent under conditions which would normally permit the fusion of the $CD4^+$ cell to the cell expressing the HIV-1 envelope glycoprotein on its surface in the absence of the agent, the first and second dyes being selected so as to allow resonance energy transfer between the dyes;

(b) exposing the product of step (a) to conditions which would result in resonance energy transfer if fusion has occurred; and

(c) determining whether there is a reduction of resonance energy transfer, when compared with the resonance energy transfer in the absence of the agent;

(d) contacting (i) a second appropriate $CD4^+$ cell, which is labeled with a first dye, with (ii) a cell expressing an HIV-1 envelope glycoprotein of a T cell-tropic isolate of HIV-1 on its surface, which is labeled with a second dye, in the presence of an excess of the agent under conditions which would normally permit the fusion of the $CD4^+$ cell to the cell expressing the HIV-1 envelope glycoprotein on its surface in the absence of the agent, the first and second dyes being selected so as to allow resonance energy transfer between the dyes;

(e) exposing the product of step (d) to conditions which would result in resonance energy transfer if fusion has occurred;

(f) determining whether there is a reduction of resonance energy transfer, when compared with the resonance energy transfer in the absence of the agent; and

(g) comparing the determination made in step (c) with the determination made in step (f),wherein a decrease in transfer in step (c) but not in step (f) indicates that the agent is capable of specifically inhibiting fusion of the macrophage-tropic primary isolate of HIV-1 to $CD4^+$ cell, but not capable of specifically inhibiting the fusion of a T cell-tropic isolate of HIV-1 to the $CD4^+$ cell.--

--9. (New) The method of claim 7, wherein the agent is an antibody.--

--10. (New) A method of inhibiting fusion of a T cell-tropic isolate of HIV-1 to a $CD4^+$ cell susceptible to infection by a T cell-tropic isolate of HIV-1 which comprises contacting the CD4+ cell with an effective amount of an agent which is (1) capable of inhibiting fusion of a T cell-tropic isolate of HIV-1 to a $CD4^+$ cell susceptible to infection by a T cell-tropic isolate of HIV-1 but (2) not capable of inhibiting fusion of a macrophage-tropic primary isolate of HIV-1 to a $CD4^+$ cell susceptible to infection by a macrophage-tropic primary isolate of HIV-1, thereby inhibiting the fusion of the T cell-tropic isolate of HIV-1 to the $CD4^+$ cell.--

--11. (New) The method of claim 10, wherein the agent is determined to be capable of inhibiting fusion of a T cell-tropic isolate of HIV-1 to a $CD4^+$ cell but not capable of inhibiting fusion of a macrophage-tropic primary isolate of HIV-1 to a $CD4^+$ cell using a method which comprises:

(a) contacting (i) a first appropriate $CD4^+$ cell, which is labeled with a first dye, with (ii) a cell expressing an HIV-1 envelope glycoprotein of the macrophage-tropic primary isolate of HIV-1 on its surface, which is labeled with a second dye, in the presence of an excess of the agent under conditions which would normally permit the fusion of the $CD4^+$ cell to the cell expressing the HIV-1 envelope glycoprotein on its surface in the absence of the agent, the first and second dyes being selected so as to allow resonance energy transfer between the dyes;

(b) exposing the product of step (a) to conditions which would result in resonance energy transfer if fusion has occurred; and

(c) determining whether there is a reduction of resonance energy transfer, when compared with the resonance energy transfer in the absence of the agent;

(d) contacting (i) a second appropriate $CD4^+$ cell, which is labeled with a first dye, with (ii) a cell expressing an HIV-1 envelope glycoprotein of a T cell-tropic isolate of HIV-1 on its surface, which is labeled with a second dye, in the presence of an excess of the agent under conditions which would normally permit the fusion of the $CD4^+$ cell to the cell expressing the HIV-1 envelope glycoprotein on its surface in the absence of the agent, the first and second dyes being selected so as to allow resonance energy transfer between the dyes;

(e) exposing the product of step (d) to conditions which would result in resonance energy transfer if fusion has occurred;

(f) determining whether there is a reduction of resonance energy transfer, when compared with the resonance energy transfer in the absence of the agent; and

(g) comparing the determination made in step (c) with the determination made in step (f),wherein a decrease in transfer in step (f) but not in step (c) indicates that the agent is capable of specifically inhibiting fusion of the T cell-tropic isolate of HIV-1 to $CD4^+$ cell, but not capable of specifically inhibiting the fusion of the macrophage-tropic primary isolate of HIV-1 to the $CD4^+$ cell.--

--12. (New) The method of claim 10, wherein the agent is an antibody.--

In the abstract:
Please add page 67 containing the abstract of the disclosure which is attached hereto as Exhibit A.

Remarks:

Claims 1-6 are pending in the subject application. Applicants have hereinabove canceled claims 1-6 without prejudice or disclaimer to their right to pursue the subject matter of these claims in a later-filed application and added new claims 7-12. Support for these amendments may be found inter alia in the specification as follows: claims 7-8: page 19, lines 12-32; page 20, lines 28-32; pages 61-64; claim 9: page 26, line 34; claims 10-11: page 19, lines 12-32; page 20, lines 28-32; pages 61-64; claim 12: page 26, line 34. This amendment does not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested such that claims 7-12 will be pending.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invites the Examiner to telephone either of them at the number provided below.

No fee, in addition to the enclosed filing fee of $710.00, is deemed necessary in connection with the filing of this Preliminary Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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